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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/559,707	04/27/2000	John Greenwood	19141-002	2553

7590 12/18/2001

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EXAMINER	
LOEB, BRONWEN	
ART UNIT	PAPER NUMBER
1636	12

DATE MAILED: 12/18/2001

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application N .	Applicant(s)	
	09/559,707	GREENWOOD ET AL.	
	Examiner	Art Unit	
	Bronwen M. Loeb	1636	

-- The MAILING DATE of this c mmunicati n appears on the cover sheet with the correspondence address --

Peri d for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *28 September 2001* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,10,24 and 37* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,10 and 24* is/are rejected.

7)☒ Claim(s) *37* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *8* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

This action is in response to the amendment filed 28 September 2001 in which claims 2-9, 11-23 and 25-36 were cancelled and claims 1, 10, 24 and 37 were amended.

Claims 1, 10, 24 and 37 are pending.

Specification

1. The disclosure is objected to because of the following informalities: On p. 21, lines 18-19, the statement regarding OX-43 expression in aortic EC does not agree with the data in Table 1. Applicants disagree. This objection is maintained for the following reasons. On p. 21, lines 18-19, it is stated that aortic endothelium expresses OX-43 antigen. However in Table 1 in the row labeled "NON-EC CNS (OX-43)" and in the column labeled "Aortic EC base", there is a negative sign. This indicates that OC-43 is not detected on aortic endothelium.

On p. 21, line 17 there is a reference to Table 2 which would appear to be incorrect; the correct reference appears to be Table 1 since Table 2 does not recite any of the markers preceding the reference.

Appropriate correction is required.

Response to Amendment

2. The double patenting rejections of claims 1, 3-6, 8, 9, 12-16, 19, 20, 25-26, 31 and 32 have been withdrawn in view of Applicant's amendment.

The written description rejection of claims 1, 7, 9-31 and 35 under 35 USC §112, first paragraph has been withdrawn in light of Applicant's amendment.

The enablement rejection of claims 22, 23 and 26 under 35 USC §112, first paragraph has been withdrawn in light of Applicant's amendment.

The rejection of claims 1-35 under 35 USC §112, second paragraph is withdrawn in view of Applicant's amendment.

The rejection of claims 1, 9, 12, 13, 15 and 19 under 35 USC §102(b) as being anticipated by Bodnar et al has been withdrawn in view of Applicant's amendment.

The rejection of claims 1, 9, and 11 under 35 USC §102(b) as being anticipated by Dunn et al has been withdrawn in view of Applicant's amendment.

The rejection of claims 1-6, 9, and 19 under 35 USC §102(b) as being anticipated by Dutt et al has been withdrawn in view of Applicant's amendment.

The rejection of claim 35 under 35 USC §102(b) as being anticipated by Manuelli et al has been withdrawn in view of Applicant's amendment.

The rejection of claims 1, 9, 12-16, 19 and 20 under 35 USC §103(a) as being unpatentable over Bodnar et al has been withdrawn in view of Applicant's amendment.

The rejection of claims 1, 9 and 12-21 under 35 USC §103(a) as being unpatentable over Bodnar et al in view of Litchfield et al has been withdrawn in view of Applicant's amendment.

The rejection of claims 1-6, 9, 19 and 36 under 35 USC §103(a) as being unpatentable over Dutt et al has been withdrawn in view of Applicant's amendment.

3. Claim 10 stands rejected under 35 USC §112, first paragraph for lack of enablement for reasons of record and as further discussed below.

Claim 24 stands rejected under 35 USC §112, first paragraph for scope of enablement for reasons of record and as further discussed below.

New rejections necessitated by Applicant's amendment are presented below.

Response to Arguments

4. With regard to the rejection of claim 10 under 35 USC §112, first paragraph, Applicant states that they will deposit the recited cell lines upon indication of allowable subject matter. The rejection stands until Applicant deposits the cell lines or makes a statement that such deposits will be made in accordance with 37 CFR §1.803. See MPEP §2411.02.

5. With regard to the rejection of claim 24 under 35 USC §112, first paragraph for scope of enablement, Applicant's argument has been considered fully but is deemed not persuasive. Applicant states that the method is enabled for in vitro and such an enablement is all that is required as a matter of law. While the claim is enabled for in vitro, it reads on in vivo applications (i.e. gene therapy). Enablement must be commensurate with the scope of the claims. With regard to a single enabled use being all that is required as a matter of law, Applicant appears to be discussing enabled use with respect to utility under 35 USC §101, which is not the basis of the rejection. Applicant further states that the method of claim 24 is not gene therapy but rather "a method of cell transplantation". As stated in the action dated 28 March 2001, gene

therapy is the delivery of nucleic acid for a therapeutic purpose. The claim recites "a method of producing *a therapeutic polypeptide to t*reat primary or secondary ophthalmologic or neurological disorders" (emphasis added) which is achieved by a cell "comprising *an expression vector comprising a polynucleotide*" (emphasis added) which expresses the therapeutic polypeptide. Thus, the claim is not simply a method of cell transplantation but clearly encompasses gene therapy. Applicant further argues that the specification provides numerous examples for transplanting epithelial cells in to restinae of rats and cites two particular examples. While both of these examples are done in vivo, they demonstrate only the transplantation of epithelial cells. The cells in question do not comprise an expression vector encoding a therapeutic polypeptide and do express said therapeutic polypeptide to treat a disorder. Therefore, these examples do not serve to enable the claim for gene therapy. The rejection is maintained.

This rejection would be overcome if the claim were amended to recite "a method of producing a therapeutic polypeptide in vitro".

New Grounds of Rejection and Objection

Claim Objections

6. Claims 1, 24 and 37 are objected to because of the following informalities:

In claim 1, there is a period after "PEDF" in step (a) which should be comma, followed by the word "and".

In claim 24, line 4 the word "produce" should be "produces".

In claim 37, the word "Institut" is misspelled.

Appropriate correction is required.

Claim Rejections - 35 USC § 112

7. The following is a quotation of the second paragraph of 35 U.S.C. §112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

8. Claims 1, 10 and 24 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1 is vague and indefinite in reciting improper Markush language. This rejection would be overcome if the claim were amended to recite "consisting of" rather than "comprising" in both line 2 and line 5.

Claim 10 is vague and indefinite in reciting "The cell line..." and reciting two cell lines using "and". Does the cell line claimed comprise both of the recited cell lines together? If not, this rejection would be overcome by amending the claim to recite "or" rather than "and" between the two cell lines.

Claim 24 is vague and indefinite in reciting improper Markush language. This rejection would be overcome if the claim were amended to recite "consisting of" rather than "comprising" in both line 3 and line 7.

Claim 24 is vague and indefinite in reciting "the polypeptide" in line 5 and "a polypeptide" in line 6. Are these two the same or different polypeptides? If they are the same, Applicant might consider amending the claim such that the phrase "and wherein the cells of the cell line..." is inserted after the word "ARPE-19" in line 4 and the phrase

"in a biological compatible medium such that the cell line produces the polypeptide" is inserted after the words "epithelial cell line" in line 3.

Claim Rejections - 35 USC § 103

9. The following is a quotation of 35 U.S.C. §103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

10. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. §103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. §103(c) and potential 35 U.S.C. §102(e), (f) or (g) prior art under 35 U.S.C. §103(a).

11. The following rejection is applied to claim 24 only in so far as the claim is enabled.

12. Claims 1 and 24 are rejected under 35 U.S.C. §103(a) as being unpatentable over Dunn et al (Invest Ophthalmol Vis Sci (1998) 39:2744-2749). Dunn et al teaches ARPE-19 comprising an expression vector encoding FGF5. The cells were used to produce FGF5 in vitro which was purified on Laemmli gel. See entire article, particularly

p. 2745-2746. At the time the invention was made, it would have been obvious to one of ordinary skill in the art to express FGF2, rather than FGF5, using ARPE-19 cells as taught by Dunn et al. One would have been motivated to do so because Dunn et al discuss the production of FGF2 by retinal cells and notes that it is known to be a mitogen in cultured RPE cells suggesting it might have an autocrine function in vivo. Thus, one would be motivated to do express FGF2 in ARPE-19 (a good model for studies of RPE cell polarity) to study the possible role of FGF2 in autocrine survival or paracrine stimulation of the choriocapillaris.

Conclusion

Claims 1, 10 and 24 are rejected. Claims 10 and 37 are free of prior art.

Applicant's submission of an information disclosure statement under 37 CFR 1.97(c) with the fee set forth in 37 CFR 1.17(p) on 2 October 2001, and the amendments filed 28 September 2001, prompted the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL.** See MPEP §§ 609(B)(2)(i) and 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any

extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Certain papers related to this application may be submitted to Art Unit 1636 by facsimile transmission. The faxing of such papers must conform with the notices published in the Official Gazette, 1156 OG 61 (November 16, 1993) and 1157 OG 94 (December 28, 1993) (see 37 C.F.R. § 1.6(d)). The official fax telephone numbers for the Group are (703) 308-4242 and (703) 305-3014. NOTE: If Applicant does submit a paper by fax, the original signed copy should be retained by applicant or applicant's representative. NO DUPLICATE COPIES SHOULD BE SUBMITTED so as to avoid the processing of duplicate papers in the Office.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Bronwen M. Loeb whose telephone number is (703) 605-1197. The examiner can normally be reached on Monday through Friday, from 10:00 AM to 6:30 PM. A phone message left at this number will be responded to as soon as possible (usually no later than the next business day after receipt by the examiner).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, George Elliott, can be reached on (703) 308-4003.

Any inquiry of a general nature or relating to the status of this application should be directed to Dianiece Jacobs, Patent Analyst whose telephone number is (703) 305-3388.

Bronwen M. Loeb, Ph.D.
Patent Examiner
Art Unit 1636

December 14, 2001

REMY YUCEL, PH.D
PRIMARY EXAMINER